Surrey and Borders Partnership NHS
NHS Foundation Trust

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NHS

Surrey (East Surrey CCG, Guildford & Waverley CCG, North West Surrey CCG, Surrey Downs CCG & Surrey Heath)

SHARED CARE PRESCRIBING GUIDELINE

CHOLINESTERASE INHIBITORS: DONEPEZIL, GALANTAMINE AND RIVASTIGMINE

Prescribing Clinical Network classification: Amber

N.B. The eligibility criteria included here apply to new patients commencing treatment under this guideline & not to existing patients whose treatment was initiated under the previous version. However, monitoring and discontinuation criteria apply to all patients.

NOTES to the GP

Amber drugs: Prescribing to be initiated by a hospital specialist (or if appropriate by a GP with specialist interest) but with the potential to transfer to primary care. The expectation is that these guidelines should provide sufficient information to enable GPs to be confident to take clinical and legal responsibility for prescribing these drugs**.**

The questions below will help you confirm this:

- Is the patient's condition predictable?
- Do you have the relevant knowledge, skills and access to equipment to allow you to monitor treatment as indicated in this shared care prescribing guideline?
- Have you been provided with relevant clinical details including monitoring data?

If you can answer YES to all these questions (after reading this shared care guideline), then it is appropriate for you to accept prescribing responsibility. Sign and return a copy of pages 8/9 to the requesting consultant at the Acute Trust. Until the requesting consultant at the Acute Trust has received a signed copy of pages 8/9 indicating that shared care has been agreed all care (including prescribing) remains with the consultant at the Acute Trust.

If the answer is NO to any of these questions, you should not accept prescribing responsibility. You should write to the consultant outlining your reasons for NOT prescribing. If you do not have the confidence to prescribe, we suggest you discuss this with your local Trust/specialist service, which will be willing to provide training and support. If you still lack the confidence to accept clinical responsibility, you still have the right to decline. Your PCT pharmacist will assist you in making decisions about shared care.

Prescribing unlicensed medicines or medicines outside the recommendations of their marketing authorisation alters (and probably increases) the prescriber's professional responsibility and potential liability. The prescriber should be able to justify and feel competent in using such medicines.

The patient's best interests are always paramount

The GP has the right to refuse to agree to shared care, in such an event the total clinical responsibility will remain with the consultant

Information

Reason for Update: Expiry of current agreement		Prepared by:
Valid from:	Review date:	Approved by:
Version: 2.4	Supersedes version:	Approved by:

This information sheet does not replace the SPC, which should be read in conjunction with this guidance. Prescribers should also refer to the appropriate paragraph in the current edition of the BNF.

Links to the relevant SPC websites:
Donepezil: http://www.medicines.org.uk/emc/medicine/577
Galantamine: http://www.medicines.org.uk/emc/medicine/10335
Rivastigmine oral: http://www.medicines.org.uk/emc/medicine/1284
Rivastigmine patch: http://www.medicines.org.uk/emc/medicine/20232

Dose:
All three drugs cause dose related cholinergic side effects. They should be started at a lower dose and the dose increased gradually according to response and tolerance to side effects.

Drug	Dose
Donepezil	5mg at bedtime (to minimise risks of side effects), increasing to 10mg daily after one month. Maximum dose 10mg
Galantamine	4mg twice daily for 4 weeks, then increase to 8mg twice daily for a further 4 weeks. This can then be increased to 12mg twice daily. Maintenance dose 8-12mg twice daily with food. Modified release form, maintenance dose 16 -24mg once daily
Rivastigmine **Rivastigmine Patch**	1.5mg twice daily, increase at a minimum of two weekly intervals by 1.5mg twice daily according to response and tolerance to a usual range of 3-6mg twice daily, swallowed whole. Incidence of side effects may be reduced by slower increases in dose at intervals of at least 4 weeks. Maximum dose 6mg twice daily Initially apply 4.6mg/24 hour patch to clean, dry, non-hairy, non-irritated skin on back, upper arm or chest, removing after 24 hours and siting a replacement patch on a different area (avoid using the same area for 14 days): if well tolerated increase to 9.5mg/24 hour patch daily after no less than 4 weeks: if patch not applied for more than several days treatment should be restarted with 4.6mg/24 hour patch. Note: when switching a patient from oral to transdermal therapy patients taking 3-6mg daily should be prescribed the 4.6mg/24hour patch; patients taking 9mg daily who do not tolerate the dose well should be prescribed the 4.6mg/24 hour patch while those taking 9mg daily who tolerate the dose well should be prescribed the 9.5mg/24 hour patch; patients taking 12mg daily should be prescribed the 9.5mg/24 hour patch. The first patch should be applied on the day following the last oral dose.

Cautions:
Donepezil:

- Sick sinus syndrome or other supraventricular conduction abnormalities
- Susceptibility to peptic ulcers
- Asthma, COPD
- Concomitant antipsychotic treatment: increased risk of neuroleptic malignant syndrome
- Anaesthesia
- Potential to cause generalised convulsions
- May cause bladder outflow obstruction
- Potential to induce or exacerbate EPSE
- Caution in mild to moderate hepatic impairment; no information for severe impairment

Galantamine:

- Cardiac disease including sick sinus syndrome or other supraventricular conduction abnormalities, unstable angina, congestive heart failure
- Electrolyte disturbances
- Susceptibility to peptic ulcers
- Asthma, COPD, pulmonary infection
- Avoid in urinary retention, gastro-intestinal obstruction and while recovering from bladder or gastro-intestinal surgery
- History of seizures
- Anaesthesia
- Lower initial and maintenance doses in moderate hepatic impairment; avoid in severe impairment
- Avoid if eGFR < 9mL/minute

Rivastigmine:

- Gastric or duodenal ulcers (or susceptibility to ulcers)
- Monitor body-weight
- Sick sinus syndrome, conduction abnormalities
- History of asthma or COPD
- History of seizures
- Bladder outflow obstruction
- Potential to induce or exacerbate EPSE
- Risk of fatal overdose with patch administration errors
- Skin application site reactions with patches
- Monitor for increase in adverse effects in patients weighing < 50kg
- Titrate according to individual tolerability in mild to moderate hepatic impairment; use with caution in severe impairment – no information available
- Titrate according to individual tolerability in renal impairment

Contraindications:

Donepezil:

- Hypersensitivity to donepezil hydrochloride, piperidine derivatives, or to any excipients
- Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption

Galantamine:

- Hypersensitivity to the active substance or to any of the excipients
- Since no data are available on the use of galantamine in patients with severe hepatic (Child-Pugh score greater than 9) and severe renal (creatinine clearance less than 9 ml/min) impairment, galantamine is contraindicated in these populations
- Patients who have both significant renal and hepatic dysfunction
- Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption

Rivastigmine:

- Hypersensitivity to the active substance, to other carbamate derivatives or to any of the excipients
- Previous history of application site reactions suggestive of allergic contact dermatitis with rivastigmine patch

Interactions:

- **Anaesthetics:** potentiation of succinylcholine type muscle relaxation during anaesthesia
- **Anticholinergic drugs:** cholinesterase inhibitors may interfere with the action of anticholinergic drugs and should not be given concomitantly with other cholinomimetic drugs.
- **Cytochrome p450:** donepezil and galantamine show decreased metabolism with potent CYP2D6 inhibitors (paroxetine, fluoxetine, fluvoxamine and quinidine) and potent CYP3A4 inhibitors (ketoconazole, erythromycin and itraconazole) thus patients may experience an increased incidence of cholinergic side effects predominately nausea and vomiting.

- **Enzyme inducers**, such as rifampicin, phenytoin, carbamazepine and alcohol may reduce the levels of donepezil. Since the magnitude of the inhibition or induction is unknown, such drug combinations should be used with care

Side effects:

Side effect	Donepezil	Galantamine	Rivastigmine
Common cold	√√√		
Rhinitis		√√√	
Hypokalaemia		√	
Anorexia	√√√	√√√	√√√
Hallucinations	√	√	√
Agitation	√√√	√	√√√
Aggressive Behaviour	√√√	√	
Insomnia	√√√	√√√	√√
Depression			√√
Confusion		√√√	√√√
Dizziness	√√√	√√√	√√√
Somnolence		√√√	√√√
Syncope	√√√	√√	√√
Convulsions	√√	√√	√
Extrapyramidal symptoms	√	√	√
Bradycardia	√	√	√
Sino-atrial block	√		
Atrioventricular block	√	√	√
Angina pectoris			√
Hypotension		√	
Diarrhoea	√√√	√√√	√√√
Vomiting	√√√	√√√	√√√
Nausea	√√√	√√√	√√√
Abdominal pain	√√√	√√√	√√√
GI haemorrhage	√√	√	√
Gastric and duodenal ulcers	√√		√
Dysphagia		√	
Pancreatitis			√
Hepatitis / liver dysfunction	√		√
Rash	√√√	√	√
Pruritus	√√√		
Muscle cramps	√√√		
Urinary incontinence	√√√		
Urinary tract infections		√√√	√
Headache	√√√	√√√	√√√
Fatigue	√√√	√√√	√√√

√ - rare √√ - uncommon √√√ - common

Criteria for Use

NICE (Technology Appraisal TA217) (updated March 2011) states that:

Cholinesterase inhibitors are recommended as an option for managing Alzheimer's disease for people with:

- Mild to moderate Alzheimer's disease

RESPONSIBILITIES and ROLES

	Specialist responsibilities
1	Confirm the probable diagnosis of a dementing illness.
2	Ensure all the necessary tests are undertaken (see under GPs responsibilities for initial tests required before referral).
3	To assess the suitability of patient for cholinesterase inhibitor treatment
4	To discuss the aims, benefits and side effects of treatment with the patient as well as their role
5	Explain to the patient their treatment plan including the dosing schedule
6	Carers' views on the patient's condition at baseline should be sought.
7	Discuss implications of diagnosis, treatment and discontinuation of treatment with carers before treatment is initiated and before sharing care with GP.
8	Initiate treatment and prescribe until a stable dose regimen is established.
9	To initiate therapy by prescribing for a minimum of 3 months
10	Monitor and evaluate response to treatment, including adverse drug reactions, with the patient and to continue / discontinue treatment in line with agreed treatment plan
11	Undertake further assessment 3 months after reaching maintenance dose before requesting GP to continue prescribing under this shared care agreement.
12	Discuss the possibility of shared care with the patient and ensure they understand the plan for their subsequent treatment
13	Supply GP with summary of patient review (including anticipated length of treatment) and a copy of the shared care guideline recommending that a shared care arrangement is initiated.
14	Review the patient's condition at least annually to ensure continuing benefit. Evaluate adverse drug reactions reported by GP, patient or carer.
15	Advise GP if treatment is to discontinue at any point.
16	Inform GP if patient does not attend planned follow-up.
17	Accept referrals back from the GP in a timely manner.

	General Practitioner responsibilities
1	Initial referral to secondary care on suspicion of Alzheimer's disease after carrying out the following tests: U&Es, LFTs, TFTs, MSU, glucose, lipid profile, bone profile, FBC, B12 and folate, ESR
2	Subsequent prescribing of cholinesterase inhibitors at the dose recommended.
3	Monitor any side effects of medication and check for interactions with other drugs.
4	Liaise with the Specialist Team if any problems arise.

	Patient's / Carer's role
1	Ask the specialist or GP for information, if he or she does not have a clear understanding of the treatment.
2	Share any concerns in relation to treatment with cholinesterase inhibitors.
3	Tell the specialist or GP of any other medication being taken, including over-the-counter products.
4	Read the patient information leaflet included with your medication and report any side effects or concerns you have to the specialist or GP

BACK-UP ADVICE AND SUPPORT

Contact details	Specialist	Telephone No.	Email address: (NHS NET)
Specialist:			
Hospital Pharmacy:			
Out of hours contact:			

SHARED CARE PRESCRIBING GUIDELINE

CHOLINESTERASE INHIBITORS: DONEPEZIL, GALANTAMINE AND RIVASTIGMINE

Agreement for transfer of prescribing to GP

Patient details / addressograph:

Name……..

Address……..
……..
……..

DOB…….

Hospital No…….

Drug Name:	**Dose/frequency:**

The following tests, investigations have been carried out: CAT ☐, MRI ☐ and SPECT ☐**.**
The patient shows signs of dementia with evidence of deterioration in 2 or more areas of cognition (minimum duration 6 months with progressive deterioration of memory and other cognitive functions), and absence of systemic disease or brain disorders.

Probable Diagnosis

- Alzheimer's disease — Yes / No
- Mixed Alzheimer's disease / vascular dementia — Yes / No

- If "No", are there non-cognitive symptoms and/or behaviour that challenges — Yes / No
- If "No" is there evidence of Lewy Body dementia — Yes / No

Severity of Alzheimer's disease:

Cognitive Assessment Score **(where appropriate):**

At the 3 month assessment the patient had been offered, accepted and tolerated treatment. I will arrange for this patient to be reviewed at least annually. I recommend that the drug as indicated in the box above should be continued. If you are in agreement to continue prescribing please sign below and fax back to ……

Agreement to end treatment will be reached by consensus between consultant, GP, patient and carer.

Date initiated:…….

At the last patient review the drug appeared to be effectively controlling symptoms/ providing benefit: Yes / No

The patients has now been stabilised on a dose of: ……..

I will arrange to review this patient regularly. Date of next clinic appointment:……

Consultant: Address: Contact Number		**Agreement to shared care, to be signed by GP and Consultant.** **Consultant Signature:** **……..** **Date:**

GP: Address: Contact Number	**GP Signature:** …… **Date:**
Main Carer: Contact Number:	**If shared care is agreed and GP has signed above please return a copy of this page to the requesting consultant or alternatively fax to:** **Acute Trust please insert appropriate Fax Number**:
Key worker if appropriate: Contact Number:	